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NEWS 10 SEP 01 New pricing for the Save Answers for SciFinder Wizard within  
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NEWS 14 OCT 28 KOREAPAT now available on STN  
  
NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004  
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=> s (factor VIII-vWF-complex)
L1          98 (FACTOR VIII-VWF-COMPLEX)
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=> s l1 and specific activity
      10 FILES SEARCHED...
L2          24 L1 AND SPECIFIC ACTIVITY
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=> s l1 and vWF activity
L3          13 L1 AND VWF ACTIVITY
```

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=> d l3 ti abs ibib tot
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L3  ANSWER 1 OF 13      MEDLINE on STN
TI  Factor VIII, von Willebrand factor and the risk of major ischaemic heart
    disease in the Caerphilly Heart Study.
AB  The relationships of three measurements of the factor VIII/von Willebrand
    factor (VWF) complex (factor VIII activity, FVIIIc (one-stage assay); VWF
```

antigen, VWF Ag (ELISA); and VWF activity, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r = 0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P = 0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the factor VIII/VWF complex and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999250512 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10233372  
TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AUTHOR: Rumley A; Lowe G D; Sweetnam P M; Yarnell J W; Ford R P  
CORPORATE SOURCE: University Department of Medicine, Glasgow Royal Infirmary, Glasgow, UK.  
SOURCE: British journal of haematology, (1999 Apr) 105 (1) 110-6.  
JOURNAL CODE: 0372544. ISSN: 0007-1048.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199906  
ENTRY DATE: Entered STN: 19990618  
Last Updated on STN: 19990618  
Entered Medline: 19990610

L3 ANSWER 2 OF 13 USPATFULL on STN

TI Haemostatically active preparation containing vwf and method for the production thereof  
AB A process for preparing a hemostatically active preparation containing von Willebrand factor (vWF) from a fraction of human plasma by chromatographic purification of a vWF-containing plasma fraction on an anion-exchange material which has the anion-exchanging groups on grafted polymeric structures (tentacle materials), collecting a vWF-containing fraction, followed by purification of said fraction using gel permeation to prepare a purified thermally stable vWF-containing preparation; and heating the preparation for inactivating viruses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:200928 USPATFULL  
TITLE: Haemostatically active preparation containing vwf and method for the production thereof  
INVENTOR(S): Josic, Djuro, Vienna, AUSTRIA  
Stadler, Monika, Wienerherberg, AUSTRIA  
Gruber, Gerhard, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003138913	A1	20030724
APPLICATION INFO.:	US 2002-257375	A1	20021017 (10)
	WO 2001-EP3819		20010404

NUMBER	DATE
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PRIORITY INFORMATION: EP 2000-108430 20000418  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: JACOBSON HOLMAN PLLC, 400 SEVENTH STREET N.W., SUITE  
600, WASHINGTON, DC, 20004  
NUMBER OF CLAIMS: 15  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 1 Drawing Page(s)  
LINE COUNT: 222  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 13 USPATFULL on STN  
TI Purification of von-Willebrand factor by cation exchanger chromatography  
AB Disclosed are a method of recovering vWF in which vWF at a low salt  
concentration is bound to a cation exchanger and vWF having a high  
specific activity is recovered by fractionated elution, as well as a  
preparation having purified vWF obtainable by this method.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:268871 USPATFULL  
TITLE: Purification of von-Willebrand factor by cation  
exchanger chromatography  
INVENTOR(S): Fischer, Bernhard, Vienna, AUSTRIA  
Schonberger, Oyvind L., Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Fiedler, Christian, Vienna, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, AUSTRALIA (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6465624	B1	20021015
	WO 9838219		19980903
APPLICATION INFO.:	US 1999-367460		19991021 (9)
	WO 1998-AT34		19980218
			19991021 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-337	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Townsend and Townsend and Crew LLP	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	726	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L3 ANSWER 4 OF 13 USPATFULL on STN  
TI Method of chromatographically purifying or fractionating, respectively,  
von Willebrand factor from a VWF-containing starting material  
AB Disclosed is a method of chromatographically purifying or fractionating,  
respectively, von Willebrand factor (vWF) from a vWF-containing starting  
material, comprising the following steps:

adsorbing the vWF from the starting material on avid collagen  
immobilized on a carrier,

separating the non-adsorbed portion and, optionally, washing the carrier,

eluting the vWF from immobilized collagen, and

recovering the purified vWF, as well as a pharmaceutical preparation comprising biologically active vWF which is bound to collagen in a stable manner.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:160854 USPATFULL  
TITLE: Method of chromatographically purifying or fractionating, respectively, von Willebrand factor from a vWF-containing starting material  
INVENTOR(S): Siekmann, Juergen, Vienna, AUSTRIA  
Turecek, Peter, Klosterneuburg, AUSTRIA  
Schwarz, Hans-Peter, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, AUSTRIA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6414125	B1	20020702
	WO 9833820		19980806
APPLICATION INFO.:	US 1999-355865		19991021 (9)
	WO 1998-AT20		19980130
			19991021 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-176	19970204
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Townsend and Townsend and Crew LLP	
NUMBER OF CLAIMS:	47	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	659	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 13 USPATFULL on STN  
TI Method for purifying factor vWF-complex by means of cation exchange chromatography  
AB There is disclosed a method of recovering **factor VIII /vWF-complex** which is characterized in that **factor VIII/vWF-complex** from a protein solution is bound to a cation exchanger and is recovered by step-wise elution of **factor VIII/vWF-complex**, which particularly contains high-molecular vWF multimers, as well as a **factor VIII/vWF-complex** obtainable by means of cation exchange chromatography.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:112884 USPATFULL  
TITLE: Method for purifying factor vWF-complex by means of cation exchange chromatography  
INVENTOR(S): Mitterer, Artur, Mannsdorf, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA

Schonberger, Oyvind L., Vienna, AUSTRIA  
Thomas-Urban, Kathrin, Freiburg, GERMANY, FEDERAL  
REPUBLIC OF  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002058625	A1	20020516
APPLICATION INFO.:	US 2001-3621	A1	20011102 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-367459, filed on 8 May 2000, PENDING A 371 of International Ser. No. WO 1998-AT43, filed on 27 Feb 1998, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-338	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	663	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L3 ANSWER 6 OF 13 USPATFULL on STN  
TI Stable **factor VIII / vWF-complex**  
AB There are disclosed a stable **factor VIII/vWF-complex**, particularly comprising high-molecular vWF multimers, being free from low-molecular vWF molecules and from proteolytic vWF degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:43190 USPATFULL  
TITLE: Stable **factor VIII / vWF-complex**  
INVENTOR(S): Fischer, Bernhard, Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002025556	A1	20020228
APPLICATION INFO.:	US 2001-849484	A1	20010507 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-142768, filed on 6 Nov 1998, GRANTED, Pat. No. US 6228613 A 371 of International Ser. No. WO 1997-AT55, filed on 13 Mar 1997, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006	
NUMBER OF CLAIMS:	43	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	1141	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 13 USPATFULL on STN

TI Stable factor VIII/von Willebrand factor complex

AB There are disclosed a stable **factor VIII/vWF**  
-**complex**, particularly comprising high-molecular vWF  
multimers, being free from low-molecular vWF molecules and from  
proteolytic vWF degradation products, as well as a method of producing  
this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:67424 USPATFULL

TITLE: Stable factor VIII/von Willebrand factor complex

INVENTOR(S): Fischer, Bernhard, Vienna, Austria  
Mitterer, Artur, Mannsdorf, Austria  
Dorner, Friedrich, Vienna, Austria  
Eibl, Johann, Vienna, Austria

PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, Austria (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6228613	B1	20010508
	WO 9734930		19970925
APPLICATION INFO.:	US 1998-142768		19981106 (9)
	WO 1997-AT55		19970313
			19981106 PCT 371 date
			19981106 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	40	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	1098	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN

TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart  
disease in the Caerphilly Heart Study.

AB The relationships of three measurements of the factor VIII/von Willebrand  
factor (VWF) complex (factor VIII activity. FVIIIc (one-stage assay); VWF  
antigen, VWF Ag (ELISA); and **VWF activity**, VWF act,  
measured by a recently-developed ELISA) to major ischaemic heart disease  
(IHD) events were studied in 1997 men aged 49-65 years, in the second  
phase of the Caerphilly Heart Study. These variables were related using  
logistic regression analysis to myocardial infarction or IHD death, which  
occurred in 129 men during an average follow-up period of 61 months. All  
three measurements were highly correlated ( $r=0.63-0.77$ ), and each was  
significantly associated with incident major IHD on univariate analyses  
(relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  
 $P=0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk  
factors and for baseline IHD. Neither FVIIIc nor VWF act was  
significantly related to incident IHD following adjustment for VWF Ag. We  
therefore suggest that the associations between these three measurements  
of the **factor VIII/VWF complex** and  
incident IHD might have at least three explanations: VWF Ag is a marker of

arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999:261609 BIOSIS  
DOCUMENT NUMBER: PREV199900261609  
TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AUTHOR(S): Rumley, A.; Lowe, G. D. O. [Reprint author]; Sweetnam, P. M.; Yarnell, J. W. G.; Ford, R. P.  
CORPORATE SOURCE: University Department of Medicine, Glasgow Royal Infirmary, 10 Alexandra Parade, Glasgow, G31 2ER, UK  
SOURCE: British Journal of Haematology, (April, 1999) Vol. 105, No. 1, pp. 110-116. print.  
CODEN: BJHEAL. ISSN: 0007-1048.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Jul 1999  
Last Updated on STN: 2 Jul 1999

L3 ANSWER 9 OF 13 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
TI Recovering high purity Factor-VIII/von Willebrand factor complexes; from plasma by bonding to immobilized monoclonal antibody obtained by hybridoma construction; affinity chromatography  
AN 1987-10591 BIOTECHDS  
AB Factor-VIII/von Willebrand factor (vWF) complexes for therapeutic use are produced by (a) adsorbing the complex in physiological medium on a monoclonal antibody able to release the complex at pH 8.5-10.5; (b) releasing the complex using an elution medium at that pH having no effect on its function but able to dissociate bonds between monoclonal antibody and the complex, and (c) collecting the purified complex. Preferably, the antibody is linked to a solid adsorbent and is used in several cycles. The monoclonal antibody is derived from a hybridoma obtained by hybridization of mouse X63 myeloma cells and splenocytes from a BALB/c mouse immunized with **Factor-VIII/vWF complex**. The product has both hemophilic A and **VWF activity**, and is obtained with a high degree of purity. (4pp)

ACCESSION NUMBER: 1987-10591 BIOTECHDS  
TITLE: Recovering high purity Factor-VIII/von Willebrand factor complexes; from plasma by bonding to immobilized monoclonal antibody obtained by hybridoma construction; affinity chromatography  
PATENT ASSIGNEE: Immunotech  
PATENT INFO: US 4670543 2 Jun 1987  
APPLICATION INFO: US 1985-777335 18 Sep 1985  
PRIORITY INFO: FR 1984-14480 18 Sep 1984  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1986-093996 [14]

L3 ANSWER 10 OF 13 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN  
TI Compsns. containing antibodies directed against blood clotting factors - for production of animal models for clotting disorders or for treating clotting disorders.  
AN 1997-022856 [03] WPIDS  
AB EP 747060 A UPAB: 19970115  
Anti-plasma antibody compsn. for the treatment of a mammal is capable of directly or indirectly inhibiting and/or eliminating several blood [clotting] factors.  
Also claimed is a mammal with a blood clotting disorder induced by a compsn. as described above.  
USE - The compsn. is used for the creation of animal models for clotting factor deficiencies, e.g. haemophilia, especially von



Willebrand-Juergens syndrome. The animal models are useful for evaluating substances for treating clotting disorders. Compsns. containing antibodies directed against von Willebrand factor (vWF) or **factor VIII/vWF complex**, are used for the treatment or prevention of conditions associated with thrombocyte aggregation resulting from abnormal **vWF activity**, e.g. haemolytic uraemic syndrome, adult respiratory distress syndrome or arteriosclerosis. The compsns. can be used for determining the bleeding characteristics of a mammal by inducing bleeding, collecting blood fractions, determining the haemoglobin content of the fractions and determining the cumulative blood loss and/or bleeding kinetics (all claimed).

Dwg.6/7

ACCESSION NUMBER: 1997-022856 [03] WPIDS  
 DOC. NO. CPI: C1997-007350  
 TITLE: Compsns. containing antibodies directed against blood clotting factors - for production of animal models for clotting disorders or for treating clotting disorders.  
 DERWENT CLASS: B04  
 INVENTOR(S): EIBL, J; SCHWARZ, H P; TURECEK, P  
 PATENT ASSIGNEE(S): (IMMO) IMMUNO AG  
 COUNTRY COUNT: 14  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 747060	A2	19961211	(199703)*	GE	18
R: AT BE CH DE DK ES FI FR GB IT LI NL SE					
EP 747060	A3	19970507	(199731)		
AT 9500987	A	19980415	(199820)		
US 5804159	A	19980908	(199843)		
AT 404429	B	19981015	(199846)		

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 747060	A2	EP 1996-890096	19960604
EP 747060	A3	EP 1996-890096	19960604
AT 9500987	A	AT 1995-987	19950609
US 5804159	A	US 1996-663031	19960607
AT 404429	B	AT 1995-987	19950609

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
AT 404429	B Previous Publ.	AT 9500987

PRIORITY APPLN. INFO: AT 1995-987 19950609

L3 ANSWER 11 OF 13 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
 AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (factor VIII activity, FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and **VWF activity**, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r = 0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses

(relative odds in highest fifth compared to lowest fifth, 1.68-1.90; P=0.028-0.006) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999150325 EMBASE  
TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AUTHOR: Rumley A.; Lowe G.D.O.; Sweetnam P.M.; Yarnell J.W.G.; Ford R.P.  
CORPORATE SOURCE: Prof. G.D.O. Lowe, University Department of Medicine, Glasgow Royal Infirmary, 10 Alexandra Parade, Glasgow G31 2ER, United Kingdom  
SOURCE: British Journal of Haematology, (1999) 105/1 (110-116).  
Refs: 24  
ISSN: 0007-1048 CODEN: BJHEAL  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
025 Hematology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L3 ANSWER 12 OF 13 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN  
TI Compsns. containing antibodies directed against blood clotting factors - for production of animal models for clotting disorders or for treating clotting disorders.

AN 1997-022856 [03] WPIX

AB EP 747060 A UPAB: 19970115

Anti-plasma antibody compsn. for the treatment of a mammal is capable of directly or indirectly inhibiting and/or eliminating several blood [clotting] factors.

Also claimed is a mammal with a blood clotting disorder induced by a compsn. as described above.

USE - The compsn. is used for the creation of animal models for clotting factor deficiencies, e.g. haemophilia, especially von Willebrand-Juergens syndrome. The animal models are useful for evaluating substances for treating clotting disorders. Compsns. containing antibodies directed against von Willebrand factor (vWF) or **factor VIII/vWF complex**, are used for the treatment or prevention of conditions associated with thrombocyte aggregation resulting from abnormal **vWF activity**, e.g. haemolytic uraemic syndrome, adult respiratory distress syndrome or arteriosclerosis. The compsns. can be used for determining the bleeding characteristics of a mammal by inducing bleeding, collecting blood fractions, determining the haemoglobin content of the fractions and determining the cumulative blood loss and/or bleeding kinetics (all claimed).

Dwg.6/7

ACCESSION NUMBER: 1997-022856 [03] WPIX

DOC. NO. CPI: C1997-007350

TITLE: Compsns. containing antibodies directed against blood clotting factors - for production of animal models for clotting disorders or for treating clotting disorders.

DERWENT CLASS: B04

INVENTOR(S): EIBL, J; SCHWARZ, H P; TURECEK, P

PATENT ASSIGNEE(S): (IMMO) IMMUNO AG

COUNTRY COUNT: 14

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 747060	A2	19961211	(199703)*	GE	18
R: AT BE CH DE DK ES FI FR GB IT LI NL SE					
EP 747060	A3	19970507	(199731)		
AT 9500987	A	19980415	(199820)		
US 5804159	A	19980908	(199843)		
AT 404429	B	19981015	(199846)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 747060	A2	EP 1996-890096	19960604
EP 747060	A3	EP 1996-890096	19960604
AT 9500987	A	AT 1995-987	19950609
US 5804159	A	US 1996-663031	19960607
AT 404429	B	AT 1995-987	19950609

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AT 404429	B Previous Publ.	AT 9500987

PRIORITY APPLN. INFO: AT 1995-987 19950609

L3 ANSWER 13 OF 13 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study

AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (factor VIII activity, FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and **VWF activity**, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r=0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P=0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999:358232 SCISEARCH

THE GENUINE ARTICLE: 192CP

TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study

AUTHOR: Rumley A; Lowe G D O (Reprint); Sweetnam P M; Yarnell J W G; Ford R P

CORPORATE SOURCE: UNIV GLASGOW, GLASGOW ROYAL INFIRM, DEPT MED, 10 ALEXANDRA PARADE, GLASGOW G31 2ER, LANARK, SCOTLAND (Reprint); UNIV GLASGOW, GLASGOW ROYAL INFIRM, DEPT MED, GLASGOW G31 2ER, LANARK, SCOTLAND; LLANDOUGH HOSP, MRC, EPIDEMIOLOGICAL UNIT S

WALES, PENARTH, S GLAM, WALES; SHIELD DIAGNOST LTD,  
 DUNDEE, SCOTLAND; QUEENS UNIV BELFAST, DIV EPIDEMIOLOG,  
 BELFAST, ANTRIM, NORTH IRELAND  
 COUNTRY OF AUTHOR: SCOTLAND; WALES; NORTH IRELAND  
 SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (APR 1999) Vol. 105, No.  
 1, pp. 110-116.  
 Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD,  
 OXFORD OX2 ONE, OXON, ENGLAND.  
 ISSN: 0007-1048.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE; CLIN  
 LANGUAGE: English  
 REFERENCE COUNT: 24  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

=> d his

(FILE 'HOME' ENTERED AT 11:14:23 ON 10 NOV 2004)

FILE 'MEDLINE, USPATFULL, CEABA-VTB, BIOSIS, BIOTECHDS, WPIDS, EMBASE,  
 DGENE, HCAPLUS, FSTA, JICST-EPLUS, WPIX, PROMT, BIOBUSINESS, SCISEARCH'  
 ENTERED AT 11:15:18 ON 10 NOV 2004

L1 98 S (FACTOR VIII-VWF-COMPLEX)  
 L2 24 S L1 AND SPECIFIC ACTIVITY  
 L3 13 S L1 AND VWF ACTIVITY

=> s l1 and factor VIII activity

L4 29 L1 AND FACTOR VIII ACTIVITY

=> s l1 and pharmaceutical preparation

L5 7 L1 AND PHARMACEUTICAL PREPARATION

=> d l7 ti abs ibib tot

L7 NOT FOUND

The L-number entered has not been defined in this session, or it  
 has been deleted. To see the L-numbers currently defined in this  
 session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l5 ti abs ibib tot

MISSING OPERATOR L5 TI

The search profile that was entered contains terms or  
 nested terms that are not separated by a logical operator.

=> d l5 ti abs ibib tot

L5 ANSWER 1 OF 7 USPATFULL on STN

TI Method of recovering highly purified vWF or **factor**  
**VIII/vWF-complex**

AB A method for purifying **factor VIII/vWF**  
**complex** or free vWF by immunoaffinity chromatography in a form  
 suitable for use as a medicament. **Factor VIII/**  
**vWF complex** or free vWF is recovered from an  
 immunoaffinity adsorbent by using an eluting agent containing a  
 zwitterionic species. The presence of the zwitterionic species allows  
 for the use of mild conditions throughout the preparation, facilitating  
 retention of molecular integrity, activity, and incorporation of the  
 recovered proteins into pharmaceutical preparations without the need for  
 additional stabilizers or preservatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:161896 USPATFULL

TITLE: Method of recovering highly purified vWF or  
**factor VIII/vWF-**

**complex**  
INVENTOR(S) : Mitterer, Artur, Mannsdorf, AUSTRIA  
Fiedler, Christian, Vienna, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA  
PATENT ASSIGNEE(S) : Baxter Aktiengesellschaft, Vienna, AUSTRIA (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6579723	B1	20030617
	WO 9838218		19980903
APPLICATION INFO.:	US 1999-367362		19991021 (9)
	WO 1998-AT33		19980218

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-339	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Le, Long V.	
ASSISTANT EXAMINER:	Gabel, Gailene R.	
LEGAL REPRESENTATIVE:	Townsend and Townsend and Crew LLP	
NUMBER OF CLAIMS:	51	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1046	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 7 USPATFULL on STN  
TI Purification of von-Willebrand factor by cation exchanger chromatography  
AB Disclosed are a method of recovering vWF in which vWF at a low salt concentration is bound to a cation exchanger and vWF having a high specific activity is recovered by fractionated elution, as well as a preparation having purified vWF obtainable by this method.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:268871 USPATFULL  
TITLE: Purification of von-Willebrand factor by cation exchanger chromatography  
INVENTOR(S) : Fischer, Bernhard, Vienna, AUSTRIA  
Schonberger, Oyvind L., Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Fiedler, Christian, Vienna, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA  
PATENT ASSIGNEE(S) : Baxter Aktiengesellschaft, Vienna, AUSTRALIA (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6465624	B1	20021015
	WO 9838219		19980903
APPLICATION INFO.:	US 1999-367460		19991021 (9)
	WO 1998-AT34		19980218
			19991021 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-337	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	

ASSISTANT EXAMINER: Robinson, Hope A.  
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP  
NUMBER OF CLAIMS: 22  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)  
LINE COUNT: 726  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 7 USPATFULL on STN

TI Method of chromatographically purifying or fractionating, respectively,  
von Willebrand factor from a VWF-containing starting material  
AB Disclosed is a method of chromatographically purifying or fractionating,  
respectively, von Willebrand factor (vWF) from a vWF-containing starting  
material, comprising the following steps:

adsorbing the vWF from the starting material on avid collagen  
immobilized on a carrier,

separating the non-adsorbed portion and, optionally, washing the  
carrier,

eluting the vWF from immobilized collagen, and

recovering the purified vWF, as well as a **pharmaceutical  
preparation** comprising biologically active vWF which is bound to  
collagen in a stable manner.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:160854 USPATFULL  
TITLE: Method of chromatographically purifying or  
fractionating, respectively, von Willebrand factor from  
a VWF-containing starting material  
INVENTOR(S): Siekmann, Juergen, Vienna, AUSTRIA  
Turecek, Peter, Klosterneuburg, AUSTRIA  
Schwarz, Hans-Peter, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, AUSTRIA (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6414125	B1	20020702
	WO 9833820		19980806
APPLICATION INFO.:	US 1999-355865		19991021 (9)
	WO 1998-AT20		19980130
			19991021 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-176	19970204
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Townsend and Townsend and Crew LLP	
NUMBER OF CLAIMS:	47	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	659	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 7 USPATFULL on STN  
TI Method for purifying factor vWF-complex by means of cation exchange chromatography  
AB There is disclosed a method of recovering **factor VIII /vWF-complex** which is characterized in that **factor VIII/vWF-complex** from a protein solution is bound to a cation exchanger and is recovered by step-wise elution of **factor VIII/vWF-complex**, which particularly contains high-molecular vWF multimers, as well as a **factor VIII/vWF-complex** obtainable by means of cation exchange chromatography.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:112884 USPATFULL  
TITLE: Method for purifying factor vWF-complex by means of cation exchange chromatography  
INVENTOR(S): Mitterer, Artur, Mannsdorf, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Schonberger, Oyvind L., Vienna, AUSTRIA  
Thomas-Urban, Kathrin, Freiburg, GERMANY, FEDERAL REPUBLIC OF  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002058625	A1	20020516
APPLICATION INFO.:	US 2001-3621	A1	20011102 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-367459, filed on 8 May 2000, PENDING A 371 of International Ser. No. WO 1998-AT43, filed on 27 Feb 1998, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-338	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	663	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 7 USPATFULL on STN  
TI Stable **factor VIII / vWF-complex**  
AB There are disclosed a stable **factor VIII/vWF-complex**, particularly comprising high-molecular vWF multimers, being free from low-molecular vWF molecules and from proteolytic vWF degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:43190 USPATFULL  
TITLE: Stable **factor VIII / vWF-complex**  
INVENTOR(S): Fischer, Bernhard, Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

NUMBER	KIND	DATE
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PATENT INFORMATION: US 2002025556 A1 20020228  
APPLICATION INFO.: US 2001-849484 A1 20010507 (9)  
RELATED APPLN. INFO.: Division of Ser. No. US 1998-142768, filed on 6 Nov  
1998, GRANTED, Pat. No. US 6228613 A 371 of  
International Ser. No. WO 1997-AT55, filed on 13 Mar  
1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006	
NUMBER OF CLAIMS:	43	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	1141	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L5 ANSWER 6 OF 7 USPATFULL on STN  
TI Highly purified factor VIII complex  
AB There is disclosed a highly purified complex comprising the components  
factor VIII and vWF having a specific activity of at least 70,  
preferably 100 to 300 U factor VIII:C/mg, a stable  
**pharmaceutical preparation** containing this complex as  
well as a method of producing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:185463 USPATFULL  
TITLE: Highly purified factor VIII complex  
INVENTOR(S): Schonhofer, Wolfgang, Polten, Austria  
Eibl, Johann, Vienna, Austria  
Weber, Alfred, Vienna, Austria  
Linnau, Yendra, Vienna, Austria  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, Austria (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6307032	B1	20011023
	WO 9739033		19971023
APPLICATION INFO.:	US 1998-171121		19981118 (9)
	WO 1997-AT69		19970409
			19981118 PCT 371 date
			19981118 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-667	19960412
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Schnizer, Holly	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
LINE COUNT:	509	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L5 ANSWER 7 OF 7 USPATFULL on STN  
TI Stable factor VIII/von Willebrand factor complex  
AB There are disclosed a stable **factor VIII/vWF**  
**-complex**, particularly comprising high-molecular vWF



multimers, being free from low-molecular vWF molecules and from proteolytic vWF degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:67424 USPATFULL  
TITLE: Stable factor VIII/von Willebrand factor complex  
INVENTOR(S): Fischer, Bernhard, Vienna, Austria  
Mitterer, Artur, Mannsdorf, Austria  
Dorner, Friedrich, Vienna, Austria  
Eibl, Johann, Vienna, Austria  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, Austria (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6228613	B1	20010508
	WO 9734930		19970925
APPLICATION INFO.:	US 1998-142768		19981106 (9)
	WO 1997-AT55		19970313
			19981106 PCT 371 date
			19981106 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	40	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	1098	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 11:14:23 ON 10 NOV 2004)

FILE 'MEDLINE, USPATFULL, CEABA-VTB, BIOSIS, BIOTECHDS, WPIDS, EMBASE, DGENE, HCAPLUS, FSTA, JICST-EPLUS, WPIX, PROMT, BIOBUSINESS, SCISEARCH' ENTERED AT 11:15:18 ON 10 NOV 2004

L1 98 S (FACTOR VIII-VWF-COMPLEX)  
L2 24 S L1 AND SPECIFIC ACTIVITY  
L3 13 S L1 AND VWF ACTIVITY  
L4 29 S L1 AND FACTOR VIII ACTIVITY  
L5 7 S L1 AND PHARMACEUTICAL PREPARATION

=> d l4 ti abs ibib tot

L4 ANSWER 1 OF 29 MEDLINE on STN  
TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (factor VIII activity, FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and VWF activity, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months.

All three measurements were highly correlated ( $r = 0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P = 0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999250512 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10233372  
TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AUTHOR: Rumley A; Lowe G D; Sweetnam P M; Yarnell J W; Ford R P  
CORPORATE SOURCE: University Department of Medicine, Glasgow Royal Infirmary, Glasgow, UK.  
SOURCE: British journal of haematology, (1999 Apr) 105 (1) 110-6.  
Journal code: 0372544. ISSN: 0007-1048.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199906  
ENTRY DATE: Entered STN: 19990618  
Last Updated on STN: 19990618  
Entered Medline: 19990610

L4 ANSWER 2 OF 29 MEDLINE on STN  
TI Acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma.  
AB A case of acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma is reported in a 58-year-old man. His initial factor VIII-von Willebrand factor (vWF) complex parameters included a **factor VIII activity** of 29 U/dL, a vWF protein of 17 U/dL, and a ristocetin cofactor of less than 10 U/dL. A specific factor VIII inhibitor could not be demonstrated in mixtures of his plasma and normal pooled plasma nor could immune complexes of IgG-factor VIII be detected in similar mixtures using protein A in a solid phase. Following surgical removal of the patient's tumor, all **factor VIII -vWF complex** parameters returned to normal. Immunoperoxidase stains of the lymphoid tumor cells were negative for von Willebrand protein. The patient's acquired von Willebrand's syndrome recurred approximately one year later, presumably indicative of recurrent lymphoma.

ACCESSION NUMBER: 88105876 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2447850  
TITLE: Acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma.  
AUTHOR: Rao K P; Kizer J; Jones T J; Anunciado A; Pepkowitz S H; Lazarchick J  
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston 29425.  
SOURCE: Archives of pathology & laboratory medicine, (1988 Jan) 112 (1) 47-50.  
Journal code: 7607091. ISSN: 0003-9985.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CASE REPORTS)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198801  
ENTRY DATE: Entered STN: 19900305  
Last Updated on STN: 19990129  
Entered Medline: 19880125

L4 ANSWER 3 OF 29 USPATFULL on STN

TI Delivery of bioactive compounds to an organism

AB Disclosed herein is a method of delivering a bioactive compound to an organism that involves growing individual cells in vitro under conditions that allow the formation of an organized tissue, at least a subset of the cells containing a foreign DNA sequence which mediates the production of the bioactive compound; and implanting the organized tissue into the organism, whereby the bioactive compound is produced and delivered to the organism. Also disclosed herein is an in vitro method for producing a tissue having in vivo-like gross and cellular morphology that involves providing precursor cells of the tissue; mixing the cells with a solution of extracellular matrix components to create a suspension; placing the suspension in a vessel having a three dimensional geometry approximating the in vivo gross and cellular morphology of the tissue and having attachment surfaces coupled thereto; allowing the suspension to coalesce; and culturing the cells under conditions in which the cells form an organized tissue connected to the attachment surfaces. Also disclosed herein is an apparatus for producing in vitro a tissue having in vivo-like gross and cellular morphology. This apparatus includes a vessel having a three dimensional geometry approximating the in vivo morphology of the tissue and tissue attachment surfaces coupled thereto.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2004:57008 USPATFULL  
TITLE: Delivery of bioactive compounds to an organism  
INVENTOR(S): Vandeburgh, Herman H., Providence, RI, UNITED STATES  
PATENT ASSIGNEE(S): Cell Based Delivery (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004043010	A1	20040304
APPLICATION INFO.:	US 2003-393143	A1	20030320 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-118950, filed on 17 Jul 1998, PENDING Continuation-in-part of Ser. No. US 1997-896152, filed on 17 Jul 1997, GRANTED, Pat. No. US 6503504 Continuation-in-part of Ser. No. US 1996-712111, filed on 13 Sep 1996, GRANTED, Pat. No. US 5869041 Continuation-in-part of Ser. No. US 1996-587376, filed on 12 Jan 1996, ABANDONED		

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1997-US303	19970110
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	25 Drawing Page(s)	
LINE COUNT:	3939	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 29 USPATFULL on STN

TI Method of recovering highly purified vWF or **factor VIII/vWF-complex**

AB A method for purifying **factor VIII/vWF complex** or free vWF by immunoaffinity chromatography in a form

suitable for use as a medicament. **Factor VIII/vWF complex** or free vWF is recovered from an immunoaffinity adsorbent by using an eluting agent containing a zwitterionic species. The presence of the zwitterionic species allows for the use of mild conditions throughout the preparation, facilitating retention of molecular integrity, activity, and incorporation of the recovered proteins into pharmaceutical preparations without the need for additional stabilizers or preservatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:161896 USPATFULL

TITLE: Method of recovering highly purified vWF or **factor VIII/vWF-complex**

INVENTOR(S): Mitterer, Artur, Mannsdorf, AUSTRIA  
Fiedler, Christian, Vienna, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, AUSTRIA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6579723	B1	20030617
	WO 9838218		19980903
APPLICATION INFO.:	US 1999-367362		19991021 (9)
	WO 1998-AT33		19980218

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-339	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Le, Long V.	
ASSISTANT EXAMINER:	Gabel, Gailene R.	
LEGAL REPRESENTATIVE:	Townsend and Townsend and Crew LLP	
NUMBER OF CLAIMS:	51	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1046	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 29 USPATFULL on STN

TI Method for purifying factor vWF-complex by means of cation exchange chromatography

AB There is disclosed a method of recovering **factor VIII/vWF-complex** which is characterized in that **factor VIII/vWF-complex** from a protein solution is bound to a cation exchanger and is recovered by step-wise elution of **factor VIII/vWF-complex**, which particularly contains high-molecular vWF multimers, as well as a **factor VIII/vWF-complex** obtainable by means of cation exchange chromatography.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:112884 USPATFULL

TITLE: Method for purifying factor vWF-complex by means of cation exchange chromatography

INVENTOR(S): Mitterer, Artur, Mannsdorf, AUSTRIA  
Fischer, Bernhard, Vienna, AUSTRIA  
Schonberger, Oyvind L., Vienna, AUSTRIA  
Thomas-Urban, Kathrin, Freiburg, GERMANY, FEDERAL REPUBLIC OF

Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002058625	A1	20020516
APPLICATION INFO.:	US 2001-3621	A1	20011102 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-367459, filed on 8 May 2000, PENDING A 371 of International Ser. No. WO 1998-AT43, filed on 27 Feb 1998, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1997-338	19970227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	663	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L4 ANSWER 6 OF 29 USPATFULL on STN

TI DELIVERY OF BIOACTIVE COMPOUNDS TO AN ORGANISM

AB Disclosed herein is a method of delivering a bioactive compound to an organism that involves growing individual cells in vitro under conditions that allow the formation of an organized tissue, at least a subset of the cells containing a foreign DNA sequence which mediates the production of the bioactive compound; and implanting the organized tissue into the organism, whereby the bioactive compound is produced and delivered to the organism. Also disclosed herein is an in vitro method for producing a tissue having in vivo-like gross and cellular morphology that involves providing precursor cells of the tissue; mixing the cells with a solution of extracellular matrix components to create a suspension; placing the suspension in a vessel having a three dimensional geometry approximating the in vivo gross and cellular morphology of the tissue and having attachment surfaces coupled thereto; allowing the suspension to coalesce; and culturing the cells under conditions in which the cells form an organized tissue connected to the attachment surfaces. Also disclosed herein is an apparatus for producing in vitro a tissue having in vivo-like gross and cellular morphology. This apparatus includes a vessel having a three dimensional geometry approximating the in vivo morphology of the tissue and tissue attachment surfaces coupled thereto.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:66628 USPATFULL  
TITLE: DELIVERY OF BIOACTIVE COMPOUNDS TO AN ORGANISM  
INVENTOR(S): VANDENBURGH, HERMAN H., PROVIDENCE, RI, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002037279	A1	20020328
APPLICATION INFO.:	US 1998-118950	A1	19980717 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-896152, filed on 17 Jul 1997, PENDING Continuation-in-part of Ser. No. US 1996-712111, filed on 13 Sep 1996, GRANTED, Pat. No. US 5869041		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	NIXON PEABODY LLP, ATTENTION: DAVID RESNICK, 101 FEDERAL STREET, BOSTON, MA, 02110		

NUMBER OF CLAIMS: 15  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 25 Drawing Page(s)  
LINE COUNT: 3958  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 7 OF 29 USPATFULL on STN  
TI Stable **factor VIII / vWF-complex**  
AB There are disclosed a stable **factor VIII/vWF-complex**, particularly comprising high-molecular vWF multimers, being free from low-molecular vWF molecules and from proteolytic vWF degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:43190 USPATFULL  
TITLE: Stable **factor VIII / vWF-complex**  
INVENTOR(S): Fischer, Bernhard, Vienna, AUSTRIA  
Mitterer, Artur, Mannsdorf, AUSTRIA  
Dorner, Friedrich, Vienna, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002025556	A1	20020228
APPLICATION INFO.:	US 2001-849484	A1	20010507 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-142768, filed on 6 Nov 1998, GRANTED, Pat. No. US 6228613 A 371 of International Ser. No. WO 1997-AT55, filed on 13 Mar 1997, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006	
NUMBER OF CLAIMS:	43	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	1141	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 8 OF 29 USPATFULL on STN  
TI Von willebrand factor derivatives and methods of isolating proteins that bind to von willebrand factor  
AB There is disclosed a vWF derivative comprised of vWF, immobilized on a carrier, which is characterized in that the vWF is r-vWF, as well as a method of isolating proteins which bind to vWF, by using this vWF derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:32215 USPATFULL  
TITLE: Von willebrand factor derivatives and methods of isolating proteins that bind to von willebrand factor  
INVENTOR(S): Schwarz, Hans-Peter, Vienna, AUSTRIA  
Turecek, Peter, Klosterneuburg, AUSTRIA  
Eibl, Johann, Vienna, AUSTRIA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002019036	A1	20020214

APPLICATION INFO.: US 2001-967937 A1 20011002 (9)  
RELATED APPLN. INFO.: Division of Ser. No. US 1999-319116, filed on 2 Jun  
1999, PENDING A 371 of International Ser. No. WO  
1997-AT253, filed on 19 Nov 1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-2178	19961213
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	598	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 9 OF 29 USPATFULL on STN  
TI Highly purified factor VIII complex  
AB There is disclosed a highly purified complex comprising the components  
factor VIII and vWF having a specific activity of at least 70,  
preferably 100 to 300 U factor VIII:C/mg, a stable pharmaceutical  
preparation containing this complex as well as a method of producing the  
same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:185463 USPATFULL  
TITLE: Highly purified factor VIII complex  
INVENTOR(S): Schonhofer, Wolfgang, Polten, Austria  
Eibl, Johann, Vienna, Austria  
Weber, Alfred, Vienna, Austria  
Linnau, Yendra, Vienna, Austria  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, Austria (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6307032	B1	20011023
	WO 9739033		19971023
APPLICATION INFO.:	US 1998-171121		19981118 (9)
	WO 1997-AT69		19970409
			19981118 PCT 371 date
			19981118 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-667	19960412
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Schnizer, Holly	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
LINE COUNT:	509	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 10 OF 29 USPATFULL on STN  
TI Stable factor VIII/von Willebrand factor complex  
AB There are disclosed a stable **factor VIII/vWF**  
**-complex**, particularly comprising high-molecular vWF  
multimers, being free from low-molecular vWF molecules and from  
proteolytic vWF degradation products, as well as a method of producing

this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:67424 USPATFULL  
TITLE: Stable factor VIII/von Willebrand factor complex  
INVENTOR(S): Fischer, Bernhard, Vienna, Austria  
Mitterer, Artur, Mannsdorf, Austria  
Dorner, Friedrich, Vienna, Austria  
Eibl, Johann, Vienna, Austria  
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Vienna, Austria (non-U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6228613	B1	20010508
	WO 9734930		19970925
APPLICATION INFO.:	US 1998-142768		19981106 (9)
	WO 1997-AT55		19970313
			19981106 PCT 371 date
			19981106 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	40	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	1098	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 11 OF 29 USPATFULL on STN  
TI Vectors and cell lines capable of correctly splicing exon regions  
AB A recombinant DNA vector is provided that expresses exons of genomic DNA fragments that are inserted into the vector. The vector contains a promoter and a genomic DNA fragment so characterized and configured that the vector, upon transcription in a transfected eukaryotic cell culture, expresses the corresponding RNA segment of the genomic DNA fragment free of any intron.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:101662 USPATFULL  
TITLE: Vectors and cell lines capable of correctly splicing exon regions  
INVENTOR(S): Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
Wood, William I., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5683905		19971104
APPLICATION INFO.:	US 1995-448171		19950523 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-595481, filed on 9 Oct 1990 which is a continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned		



DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Robinson, Douglas W.  
ASSISTANT EXAMINER: Wai, Thanda  
LEGAL REPRESENTATIVE: Hasak, Janet E., McNicholas, Janet M.  
NUMBER OF CLAIMS: 6  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 41 Drawing Figure(s); 32 Drawing Page(s)  
LINE COUNT: 2579  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 12 OF 29 USPATFULL on STN  
TI Preparation of functional human factor VIII and pharmaceutical treatment  
therewith  
AB Functional human factor VIII produced recombinantly is used in the  
treatment of human beings diagnosed to be deficient in factor VIII  
coagulant activity. Also provided are DNA isolates and expression  
vehicles encoding functional human factor VIII, as well as transformed  
host cells and processes for producing human factor VIII by use of  
recombinant DNA technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:83935 USPATFULL  
TITLE: Preparation of functional human factor VIII and  
pharmaceutical treatment therewith  
INVENTOR(S): Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
Wood, William I., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5668108		19970916
APPLICATION INFO.:	US 1995-447654		19950523 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-570096, filed on 20 Aug 1990, now patented, Pat. No. US 5618788 which is a continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned		

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Jacobson, Dian C.  
LEGAL REPRESENTATIVE: Hasak, Janet E.  
NUMBER OF CLAIMS: 2  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 41 Drawing Figure(s); 32 Drawing Page(s)  
LINE COUNT: 2566  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 13 OF 29 USPATFULL on STN  
TI Method of hybridization using oligonucleotide probes  
AB An improved method of hybridization with oligonucleotide probes using  
tetramethylammonium chloride is provided. The method is useful for  
screening mixtures of DNA sequences, including libraries of high DNA  
sequence complexity, with a single oligonucleotide probe or a pool of  
probes representing all possible codon choices for a short amino acid  
sequence.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:68321 USPATFULL  
TITLE: Method of hybridization using oligonucleotide probes

INVENTOR(S): Wood, William I., San Mateo, CA, United States  
Lasky, Laurence A., Sausalito, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., San Francisco, CA, United States (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5654147		19970805
APPLICATION INFO.:	US 1995-447486		19950523 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-829867, filed on 3 Feb 1992, now patented, Pat. No. US 5618789 which is a division of Ser. No. US 1990-570096, filed on 20 Aug 1990, now patented, Pat. No. US 5618788 which is a continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Jones, W. Gary		
ASSISTANT EXAMINER:	Rees, Dianne		
LEGAL REPRESENTATIVE:	Hasak, Janet E.		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	41 Drawing Figure(s); 32 Drawing Page(s)		
LINE COUNT:	2586		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 14 OF 29 USPATFULL on STN  
TI Preparation of functional human factor VIII  
AB Functional human factor VIII produced recombinantly is used in the treatment of human beings diagnosed to be deficient in factor VIII coagulant activity. Also provided are DNA isolates and expression vehicles encoding functional human factor VIII, as well as transformed host cells and processes for producing human factor VIII by use of recombinant DNA technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:44916 USPATFULL  
TITLE: Preparation of functional human factor VIII  
INVENTOR(S): Wood, William I., San Mateo, CA, United States  
Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5633150		19970527
APPLICATION INFO.:	US 1990-595481		19901009 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Jacobson, Dian C.		
LEGAL REPRESENTATIVE:	Hasak, Janet E.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	40 Drawing Figure(s); 32 Drawing Page(s)		
LINE COUNT:	2495		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 29 USPATFULL on STN  
TI Functional human factor VIII  
AB Functional human factor VIII produced recombinantly is used in the treatment of human beings diagnosed to be deficient in factor VIII coagulant activity. Also provided are DNA isolates and expression vehicles encoding functional human factor VIII, as well as transformed host cells and processes for producing human factor VIII by use of recombinant DNA technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:29446 USPATFULL  
TITLE: Functional human factor VIII  
INVENTOR(S): Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
Wood, William I., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5618789		19970408
APPLICATION INFO.:	US 1992-829867		19920203 (7)
RELATED APPLN. INFO.:	Division of Ser. No. US 1990-570096, filed on 20 Aug 1990 which is a continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Jacobson, Dian C.		
LEGAL REPRESENTATIVE:	Hasak, Janet E.		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	41 Drawing Figure(s); 32 Drawing Page(s)		
LINE COUNT:	2485		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 16 OF 29 USPATFULL on STN  
TI Preparation of functional human factor VIII and pharmaceutical treatment therewith  
AB Functional human factor VIII produced recombinantly is used in the treatment of human beings diagnosed to be deficient in factor VIII coagulant activity. Also provided are DNA isolates and expression vehicles encoding functional human factor VIII, as well as transformed host cells and processes for producing human factor VIII by use of recombinant DNA technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:29445 USPATFULL  
TITLE: Preparation of functional human factor VIII and pharmaceutical treatment therewith  
INVENTOR(S): Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
Wood, William I., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5618788		19970408
APPLICATION INFO.:	US 1990-570096		19900820 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1987-83758, filed on 7 Aug 1987, now patented, Pat. No. US 4965199 which is a continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984, now abandoned

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Jacobson, Dian C.  
LEGAL REPRESENTATIVE: Hasak, Janet E.  
NUMBER OF CLAIMS: 1  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 41 Drawing Figure(s); 32 Drawing Page(s)  
LINE COUNT: 2536  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 17 OF 29 USPATFULL on STN  
TI Preparation of functional human factor VIII in mammalian cells using methotrexate based selection  
AB A method for producing factor VIII in recombinant mammalian host cells utilizing an expression vector containing a selectable marker DNA and an amplifiable marker DNA. The initial selection is based upon the selectable marker and subsequent amplification of factor VIII DNA and amplifiable marker DNA is conducted in cells not deficient in the amplifiable marker.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 90:81726 USPATFULL  
TITLE: Preparation of functional human factor VIII in mammalian cells using methotrexate based selection  
INVENTOR(S): Capon, Daniel J., San Mateo, CA, United States  
Lawn, Richard M., San Francisco, CA, United States  
Levinson, Arthur D., Hillsborough, CA, United States  
Vehar, Gordon A., San Carlos, CA, United States  
Wood, William I., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4965199		19901023
APPLICATION INFO.:	US 1987-83758		19870807 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1984-602312, filed on 20 Apr 1984		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Teskin, Robin L.		
LEGAL REPRESENTATIVE:	Hasak, Janet E.		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 32 Drawing Page(s)		
LINE COUNT:	2416		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 18 OF 29 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
TI Regulation of **factor VIII activity** by the factor VIIa-tissue factor complex.  
AB Blood coagulation is triggered at the site of vascular damage when exposed tissue factor (TF) contacts plasma factor VIIa (fVIIa). The resulting enzyme-cofactor complex (fVIIa-TF) activates fX and fIX by limited proteolysis to generate fXa and fIXa and propagate/amplify the coagulant response. Although this is the accepted mechanism for coagulation initiation under normal conditions and has been the focus of many studies, other relatively "minor" (and thus understudied) pathways may manifest themselves and be of greater importance under various pathological

conditions in which TF has been implicated. Our previous studies have demonstrated that the fVIIa-TF complex can cleave fVIII, the essential procofactor for fIXa. While these experiments were done using recombinant fVIII in vitro and showed the product as being largely inactivated fVIII, an initial transient twofold increase in fVIIIa clotting activity was observed. This may be of import in vivo when considering the potential for TF-containing microparticles to fuse with fVIII-rich platelet microparticles as well as the recent description of alternatively-spliced TF that can localize to platelets. This possibility prompted us to examine the ability of the fVIIa-TF complex to regulate fVIII activity in plasma. Activation of fVIII was measured using fX-deficient plasma as the fVIII source in the presence or absence of fVIIa in complex with TFK165,166A (a mutant form of TF that does not support cleavage of fIX or fX). An immediate TF-dependent increase in activity of fVIIIa was observed which peaked at 5 minutes (7-10 fold maximum increase in fVIIIa activity). This elevated fVIIIa activity persisted for greater than 60 min and its appearance was not affected by inclusion of soybean trypsin inhibitor (1  $\mu$ M) or hirudin (1 U/ml), ruling out fVIII activation by the two known physiological fVIII activators factor Xa and thrombin. In addition, no measurable thrombin was detectable in assays of fVIIa-TF activation of fVIII over 60 min, and no clot was observed over this time period. As a comparison, addition of low levels of thrombin to the plasma resulted in much different kinetics with rapid appearance and decay of fVIIIa activity and formation of a clot. Assays done using the purified fVIII-vWf complex (Koate) in vitro showed similar activation kinetics by fVIIa-TF to that observed in plasma. From this data we propose that the fVIIa-TF complex can activate fVIII in plasma and that the fVIIIa activity produced is longer-lived than that obtained by fVIII activation with thrombin. Thus, activation of fVIII by the fVIIa-TF complex in this way would allow sustained low-level coagulation for much longer durations than fVIII activation by thrombin or fXa. While likely not of consequence in hemostasis, this would be expected to be of great consequence in disease states or wound-healing scenarios where such long-term interactions between these proteins can occur, thus potentially affecting a long-term prothrombotic state.

ACCESSION NUMBER: 2004:153816 BIOSIS  
DOCUMENT NUMBER: PREV200400148262  
TITLE: Regulation of **factor VIII activity** by the factor VIIa-tissue factor complex.  
AUTHOR(S): Neuenschwander, Pierre F. [Reprint Author]  
CORPORATE SOURCE: Biochemistry, University of Texas Health Center at Tyler, Tyler, TX, USA  
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 749a. print.  
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; (Meeting Poster)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 17 Mar 2004  
Last Updated on STN: 17 Mar 2004

L4 ANSWER 19 OF 29 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (**factor VIII activity**. FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and VWF activity, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the

second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r=0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P=0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999:261609 BIOSIS  
DOCUMENT NUMBER: PREV199900261609  
TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.  
AUTHOR(S): Rumley, A.; Lowe, G. D. O. [Reprint author]; Sweetnam, P. M.; Yarnell, J. W. G.; Ford, R. P.  
CORPORATE SOURCE: University Department of Medicine, Glasgow Royal Infirmary, 10 Alexandra Parade, Glasgow, G31 2ER, UK  
SOURCE: British Journal of Haematology, (April, 1999) Vol. 105, No. 1, pp. 110-116. print.  
CODEN: BJHEAL. ISSN: 0007-1048.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Jul 1999  
Last Updated on STN: 2 Jul 1999

L4 ANSWER 20 OF 29 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
TI THE RELATIONSHIP BETWEEN COAGULATION FACTOR VIII AND ABO BLOOD GROUP STATUS.  
AB Procoagulant **factor VIII activity** (VIII:C) and procoagulant antigen (VIII:Ag) levels were measured in 402 blood donors (blood group O = 182, A = 160, B = 49 and AB = 11) to determine whether the measured activity (VIII:C) of the VIII component of the factor VIII/von Willebrand **factor (VIII/vWF complex)** was reflected in the level of the antigen (VIII:Ag). Both VIII:C and VIII:Ag were significantly and similarly lower in blood group O individuals than in those of other blood groups. However, there was no significant difference between VIII:C activity and VIII:Ag levels for each of the ABO blood groups (i.e. VIII:C/VIII:Ag ratios = 1.0).

ACCESSION NUMBER: 1988:287290 BIOSIS  
DOCUMENT NUMBER: PREV198886015557; BA86:15557  
TITLE: THE RELATIONSHIP BETWEEN COAGULATION FACTOR VIII AND ABO BLOOD GROUP STATUS.  
AUTHOR(S): MCLELLAN D S [Reprint author]; KNIGHT S R; ARONSTAM A  
CORPORATE SOURCE: SCH PHARMACY AND BIOMEDICAL SCI, PORTSMOUTH POLYTECHNIC, PORTSMOUTH, HAMPSHIRE, UK  
SOURCE: Medical Laboratory Sciences, (1988) Vol. 45, No. 2, pp. 131-134.  
CODEN: MLASDU. ISSN: 0308-3616.  
DOCUMENT TYPE: Article  
FILE SEGMENT: BA  
LANGUAGE: ENGLISH  
ENTRY DATE: Entered STN: 16 Jun 1988  
Last Updated on STN: 16 Jun 1988

L4 ANSWER 21 OF 29 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI ACQUIRED VON WILLEBRAND'S SYNDROME ASSOCIATED WITH AN EXTRANODAL PULMONARY LYMPHOMA.

AB A case of acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma is reported in a 58-year-old man. His initial factor VIII-von Willebrand factor (vWF) complex parameters included a **factor VIII activity** of 29 U/dL, a vWF protein of 17 U/dL, and a ristocetin cofactor of < 10 U/dL. A specific factor VIII inhibitor could not be demonstrated in mixtures of his plasma and normal pooled plasma nor could immune complexes of IgG-factor VIII be detected in similar mixtures using protein A in a solid phase. Following surgical removal of the patient's tumor, all **factor VIII -vWF complex** parameters returned to normal. Immunoperoxidase stains of the lymphoid tumor cells were negative for von Willebrand protein. The patient's acquired von Willebrand's syndrome recurred approximately one year later, presumably indicative of recurrent lymphoma.

ACCESSION NUMBER: 1988:135066 BIOSIS  
DOCUMENT NUMBER: PREV198885069893; BA85:69893  
TITLE: ACQUIRED VON WILLEBRAND'S SYNDROME ASSOCIATED WITH AN EXTRANODAL PULMONARY LYMPHOMA.  
AUTHOR(S): RAO K P P [Reprint author]; KIZER J; JONES T J; ANUNCIADO A; PEPKOWITZ S H; LAZARCHICK J  
CORPORATE SOURCE: DEP PATHOL LAB MED, MED UNIV SOUTH CAROLINA, 171 ASHLEY AVE, CHARLESTON, SC 29425, USA  
SOURCE: Archives of Pathology and Laboratory Medicine, (1988) Vol. 112, No. 1, pp. 47-50.  
CODEN: ARPAAQ. ISSN: 0363-0153.  
DOCUMENT TYPE: Article  
FILE SEGMENT: BA  
LANGUAGE: ENGLISH  
ENTRY DATE: Entered STN: 12 Mar 1988  
Last Updated on STN: 12 Mar 1988

L4 ANSWER 22 OF 29 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

TI Carrier-fixed recombinant von Willebrand factor derivative - useful for isolating proteins binding von Willebrand factor, e.g. factor VIII, in high yield.

AN 1998-348459 [30] WPIDS

AB WO 9825969 A UPAB: 19980730

Derivative (I) of von Willebrand Factor (vWF) consists of recombinant vWF (r-vWF) immobilised on a particulate or gel carrier (II).

Also claimed are:

(1) a method for isolating vWF-binding proteins (III), comprising:  
(a) contacting a fraction containing (III) with (I) so that (III) bind with (I);

(b) removing the non-bound components, and

(c) eluting (III) from (I), and

(2) a device consisting of a container (specifically an affinity column) containing (I) and having an inlet and an outlet for liquid.

USE - The method and device are useful for removing, recovering, purifying and/or concentrating (III) contained in liquid samples, specifically fractions contained in a mammalian body fluid or cell culture sample.

(III) is e.g. glycoprotein Ib, the glycoprotein in IIb/IIIa complex, collagen, factor VIII (including recombinant derivatives and analogues), vWF antigen, vWF antibody or an enzyme recognising vWF as substrate (e.g. vWF multimerase or vWF depolymerase).

Saccharides binding vWF (e.g. heparin) can also be isolated.

Typical applications are: isolation of pure proteins with **factor VIII activity** for biochemical-analytical, diagnostic or therapeutic use; purification of vWF multimerase; extra-corporeal immuno-adsorption of anti-vWF antibodies (associated with pathological states such as auto-immune disease); or preparative recovery of mono- or poly-clonal anti-vWF antibodies for

diagnostic use.

ADVANTAGE - The affinity of (I) for (III) is higher than that of plasma vWF, so that (III) can be isolated even from solutions containing vWF (e.g. in **factor VIII-vWF complex**).

(III) can be isolated in high yield, specifically at least 80% (claimed). (I) have high stability, can be used repeatedly and retain the 'nativity' of vWF. r-vWF is readily available in high purity.

Dwg.0/2

ACCESSION NUMBER: 1998-348459 [30] WPIDS  
DOC. NO. CPI: C1998-107760  
TITLE: Carrier-fixed recombinant von Willebrand factor derivative - useful for isolating proteins binding von Willebrand factor, e.g. factor VIII, in high yield.  
DERWENT CLASS: B04 D16  
INVENTOR(S): EIBL, J; SCHWARZ, H; TURECEK, P  
PATENT ASSIGNEE(S): (IMMO) IMMUNO AG; (BAXT) BAXTER AG; (EIBL-I) EIBL J; (SCHW-I) SCHWARZ H; (TURE-I) TURECEK P  
COUNTRY COUNT: 22  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9825969	A1	19980618	(199830)*	GE	29
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CZ HU JP US					
AT 9602178	A	19990315	(199916)		
AT 405740	B	19990915	(199942)		
CZ 9902112	A3	19990915	(199945)		
EP 954533	A1	19991110	(199952)	GE	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
HU 9903789	A2	20000328	(200025)		
JP 2001506987	W	20010529	(200136)		22
US 2002019036	A1	20020214	(200214)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9825969	A1	WO 1997-AT253	19971119
AT 9602178	A	AT 1996-2178	19961213
AT 405740	B	AT 1996-2178	19961213
CZ 9902112	A3	WO 1997-AT253	19971119
		CZ 1999-2112	19971119
EP 954533	A1	EP 1997-913009	19971119
		WO 1997-AT253	19971119
HU 9903789	A2	WO 1997-AT253	19971119
		HU 1999-3789	19971119
JP 2001506987	W	WO 1997-AT253	19971119
		JP 1998-526003	19971119
US 2002019036	A1 Div ex	WO 1997-AT253	19971119
	Div ex	US 1999-319116	19990602
		US 2001-967937	20011002

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AT 405740	B Previous Publ.	AT 9602178
CZ 9902112	A3 Based on	WO 9825969
EP 954533	A1 Based on	WO 9825969
HU 9903789	A2 Based on	WO 9825969
JP 2001506987	W Based on	WO 9825969



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TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.

AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (**factor VIII activity**, FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and VWF activity, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r = 0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P=0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999150325 EMBASE

TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study.

AUTHOR: Rumley A.; Lowe G.D.O.; Sweetnam P.M.; Yarnell J.W.G.; Ford R.P.

CORPORATE SOURCE: Prof. G.D.O. Lowe, University Department of Medicine, Glasgow Royal Infirmary, 10 Alexandra Parade, Glasgow G31 2ER, United Kingdom

SOURCE: British Journal of Haematology, (1999) 105/1 (110-116).  
Refs: 24

ISSN: 0007-1048 CODEN: BJHEAL

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

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TI The relationship between coagulation factor VIII and ABO blood group status.

AB Procoagulant **factor VIII activity** (VIII:C) and procoagulant antigen (VIII:Ag) levels were measured in 402 blood donors (blood group O = 182, A = 160, B = 49 and AB = 11) to determine whether the measured activity (VIII:C) of the VIII component of the factor VIII/von Willebrand **factor** (VIII/vWF) **complex** was reflected in the level of the antigen (VIII:Ag). Both VIII:C and VIII:Ag were significantly and similarly lower in blood group O individuals than in those of other blood groups. However, there was no significant difference between VIII:C activity and VIII:Ag levels for each of the ABO blood groups (i.e. VIII:C/VIII:Ag ratios = 1.0).

ACCESSION NUMBER: 88124888 EMBASE

DOCUMENT NUMBER: 1988124888

TITLE: The relationship between coagulation factor VIII and ABO blood group status.

AUTHOR: McLellan D.S.; Knight S.R.; Aronstam A.  
CORPORATE SOURCE: School of Pharmacy and Biomedical Sciences, Portsmouth  
Polytechnic, Portsmouth, Hampshire, United Kingdom  
SOURCE: Medical Laboratory Sciences, (1988) 45/2 (131-134).  
ISSN: 0308-3616 CODEN: MLASDU  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 025 Hematology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

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on STN

TI Acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma.

AB A case of acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma is reported in a 58-year-old man. His initial factor VIII-von Willebrand factor (vWF) complex parameters included a **factor VIII activity** of 29 U/dL, a vWF protein of 17 U/dL, and a ristocetin cofactor of <10 U/dL. A specific factor VIII inhibitor could not be demonstrated in mixtures of his plasma and normal pooled plasma nor could immune complexes of IgG-factor VIII be detected in similar mixtures using protein A in a solid phase. Following surgical removal of the patient's tumor, all **factor VIII-vWF complex** parameters returned to normal. Immunoperoxidase stains of the lymphoid tumor cells were negative for von Willebrand protein. The patient's acquired Von Willebrand's syndrome recurred approximately one year later, presumably indicative of recurrent lymphoma.

ACCESSION NUMBER: 88025592 EMBASE

DOCUMENT NUMBER: 1988025592

TITLE: Acquired von Willebrand's syndrome associated with an extranodal pulmonary lymphoma.

AUTHOR: Rao K.P.P.; Kizer J.; Jones T.J.; Anunciado A.; Pepkowitz S.H.; Lazarchick J.

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC 29425, United States

SOURCE: Archives of Pathology and Laboratory Medicine, (1988) 112/1 (47-50).

ISSN: 0003-9985 CODEN: ARPAAQ

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
016 Cancer  
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

L4 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN

TI Analysis of free factor VIII antigen in commercial factor VIII concentrates

AB The association of factor VIII with von Willebrand factor (vWF) is important for protection of factor VIII against proteolytic degradation in plasma. Recently developed factor VIII preps., namely monoclonal antibody-purified factor VIII (M-factor VIII) and recombinant factor VIII, contain free form of factor VIII that is expected to form complexes with endogenous vWF after venous injection in the patients with hemophilia A. To clarify the difference of free factor VIII and **factor VIII-vWF complex** in the com. factor VIII concs., we developed a quant. assay for free factor VIII in which the sample was added to the wells of vWF-coated microtiter plates. Bound factor VIII was detected by monoclonal antibody against factor VIII,

followed by incubation with peroxidase conjugated anti-mouse IgG, then the substrate ABTS for measuring absorbance at 405 nm. When the amount of free factor VIII antigen in one unit **factor VIII activity** of recombinant factor VIII was defined as one arbitrary unit, the ELISA detected free factor VIII as low as 0.016 unit/mL. Factor VIII was incubated with vWF or plasma from a patient with severe Hemophilia A for various concns., prior to the free factor VIII assay. At saturation, the stoichiometry was one factor VIII mol. per 50 vWF monomers. Of the products of **factor VIII-vWF complex** concentrate, no free factor VIII was detected. While a M-factor VIII concentrate contained free factor VIII comprising 24% of total **factor VIII activity**. In a gel filtration experiment of M-factor VIII, 15% of the total factor VIII was eluted as free factor VIII and 77% of that was co-eluted with vWF in the void volume. The free factor VIII and the complex form of factor VIII were immunoisolated and were analyzed after SDS-PAGE by immunoblotting. The factor VIII mol. structure and the susceptibility of thrombin cleavage were indistinguishable between the two forms of factor VIII. These results suggested that free factor VIII present in the M-factor VIII concentrate forms complexes with vWF in hemophilic plasma and is involved in physiologic hemostasis.

ACCESSION NUMBER: 1997:262983 HCAPLUS  
DOCUMENT NUMBER: 126:321126  
TITLE: Analysis of free factor VIII antigen in commercial factor VIII concentrates  
AUTHOR(S): Watanabe, Jun; Arai, Morio; Kagawa, Kazuhiko; Amano, Kagehiro; Fukutake, Katsuyuki  
CORPORATE SOURCE: Dept. Clinical Pathology, Tokyo Medical College, Tokyo, 160, Japan  
SOURCE: Nippon Kessen Shiketsu Gakkaishi (1997), 8(1), 44-54  
CODEN: NKSSEL; ISSN: 0915-7441  
PUBLISHER: Nippon Kessen Shiketsu Gakkai  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

L4 ANSWER 27 OF 29 JICST-EPlus COPYRIGHT 2004 JST on STN

TI Detection and Characterization of an Anti-Factor VIII Antibody that Does Not Inhibit Biological Activity.

AB One of the major factors complicating the treatment of hemophilia A is development of factor VIII inhibitors, which represent anti-factor VIII alloantibodies. Hitherto, inhibitors have been recognized to be acquired antibodies that neutralize **factor VIII activity**, and they have been routinely measured with the Bethesda assay based on their inhibitory action on **factor VIII activity**. In the present study, the authors used immunochemical methods to investigate the properties of an anti-factor VIII antibody recovered from a patient in whom inhibitor was not detectable with the Bethesda method (.LEQ.0.4), but in whom in vivo recovery rate of factor VIII preparations was abnormally decreased to below 50%. Using a purified factor VIII preparation as an antigen, SDS-polyacrylamide-gel electrophoresis (SDS-PAGE) and Western blotting were performed, with the preparation reacted with patient plasma. As a result, the antibody was detected as an IgG antibody bound to an 80kDa factor VIII light chain band. Then, the influence exerted by this antibody on the binding of factor VIII and von Willebrand factor (vWF), which forms a non-covalent bond with factor VIII, thereby stabilizing the latter as a carrier protein and which is thought to also enhance thrombin-mediated **factor VIII activity**, was investigated. In an ELISA using anti-factor VIII monoclonal antibody as the capture antibody and anti-vWF antibody as the tag antibody, IgG (2.2mg/ml) prepared from patient plasma and a recombinant factor VIII preparation (r-F VIII) were reacted and then mixed with vWF. However, no inhibition of **factor VIII/vWF complex** formation was found. (abridged author abst.)

ACCESSION NUMBER: 920822061 JICST-EPlus

TITLE: Detection and Characterization of an Anti-Factor VIII Antibody that Does Not Inhibit Biological Activity.  
AUTHOR: KOSHIHARA KIMIHIITO; FUKUTAKE KATSUYUKI; ARAI MORIO  
CORPORATE SOURCE: Tokyo Medical College  
SOURCE: Tokyo Ika Daigaku Zasshi (Journal of Tokyo Medical College), (1992) vol. 50, no. 5, pp. 801-807. Journal Code: F0570A (Fig. 2, Tbl. 3, Ref. 20)  
CODEN: TIDZAH; ISSN: 0040-8905  
PUB. COUNTRY: Japan  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: Japanese  
STATUS: New

L4 ANSWER 28 OF 29 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN

TI Carrier-fixed recombinant von Willebrand factor derivative - useful for isolating proteins binding von Willebrand factor, e.g. factor VIII, in high yield.

AN 1998-348459 [30] WPIX

AB WO 9825969 A UPAB: 19980730

Derivative (I) of von Willebrand Factor (vWF) consists of recombinant vWF (r-vWF) immobilised on a particulate or gel carrier (II).

Also claimed are:

- (1) a method for isolating vWF-binding proteins (III), comprising:
  - (a) contacting a fraction containing (III) with (I) so that (III) bind with (I);
  - (b) removing the non-bound components, and
  - (c) eluting (III) from (I), and
- (2) a device consisting of a container (specifically an affinity column) containing (I) and having an inlet and an outlet for liquid.

USE - The method and device are useful for removing, recovering, purifying and/or concentrating (III) contained in liquid samples, specifically fractions contained in a mammalian body fluid or cell culture sample.

(III) is e.g. glycoprotein Ib, the glycoprotein in IIb/IIIa complex, collagen, factor VIII (including recombinant derivatives and analogues), vWF antigen, vWF antibody or an enzyme recognising vWF as substrate (e.g. vWF multimerase or vWF depolymerase).

Saccharides binding vWF (e.g. heparin) can also be isolated.

Typical applications are: isolation of pure proteins with **factor VIII activity** for biochemical-analytical, diagnostic or therapeutic use; purification of vWF multimerase; extra-corporeal immuno-adsorption of anti-vWF antibodies (associated with pathological states such as auto-immune disease); or preparative recovery of mono- or poly-clonal anti-vWF antibodies for diagnostic use.

ADVANTAGE - The affinity of (I) for (III) is higher than that of plasma vWF, so that (III) can be isolated even from solutions containing vWF (e.g. in **factor VIII-vWF complex**).

(III) can be isolated in high yield, specifically at least 80% (claimed). (I) have high stability, can be used repeatedly and retain the 'nativity' of vWF. r-vWF is readily available in high purity.

Dwg.0/2

ACCESSION NUMBER: 1998-348459 [30] WPIX

DOC. NO. CPI: C1998-107760

TITLE: Carrier-fixed recombinant von Willebrand factor derivative - useful for isolating proteins binding von Willebrand factor, e.g. factor VIII, in high yield.

DERWENT CLASS: B04 D16

INVENTOR(S): EIBL, J; SCHWARZ, H; TURECEK, P

PATENT ASSIGNEE(S): (IMMO) IMMUNO AG; (BAXT) BAXTER AG; (EIBL-I) EIBL J; (SCHW-I) SCHWARZ H; (TURE-I) TURECEK P

COUNTRY COUNT: 22

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9825969	A1	19980618	(199830)*	GE	29
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CZ HU JP US					
AT 9602178	A	19990315	(199916)		
AT 405740	B	19990915	(199942)		
CZ 9902112	A3	19990915	(199945)		
EP 954533	A1	19991110	(199952)	GE	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
HU 9903789	A2	20000328	(200025)		
JP 2001506987	W	20010529	(200136)		22
US 2002019036	A1	20020214	(200214)		

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9825969	A1	WO 1997-AT253	19971119
AT 9602178	A	AT 1996-2178	19961213
AT 405740	B	AT 1996-2178	19961213
CZ 9902112	A3	WO 1997-AT253	19971119
		CZ 1999-2112	19971119
EP 954533	A1	EP 1997-913009	19971119
		WO 1997-AT253	19971119
HU 9903789	A2	WO 1997-AT253	19971119
		HU 1999-3789	19971119
JP 2001506987	W	WO 1997-AT253	19971119
		JP 1998-526003	19971119
US 2002019036	A1 Div ex	WO 1997-AT253	19971119
	Div ex	US 1999-319116	19990602
		US 2001-967937	20011002

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
AT 405740	B Previous Publ.	AT 9602178
CZ 9902112	A3 Based on	WO 9825969
EP 954533	A1 Based on	WO 9825969
HU 9903789	A2 Based on	WO 9825969
JP 2001506987	W Based on	WO 9825969

PRIORITY APPLN. INFO: AT 1996-2178 19961213

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TI Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study

AB The relationships of three measurements of the factor VIII/von Willebrand factor (VWF) complex (**factor VIII activity**, FVIIIc (one-stage assay); VWF antigen, VWF Ag (ELISA); and VWF activity, VWF act, measured by a recently-developed ELISA) to major ischaemic heart disease (IHD) events were studied in 1997 men aged 49-65 years, in the second phase of the Caerphilly Heart Study. These variables were related using logistic regression analysis to myocardial infarction or IHD death, which occurred in 129 men during an average follow-up period of 61 months. All three measurements were highly correlated ( $r=0.63-0.77$ ), and each was significantly associated with incident major IHD on univariate analyses (relative odds in highest fifth compared to lowest fifth, 1.68-1.90;  $P=0.028-0.006$ ) and on multivariate analyses adjusting for major IHD risk factors and for baseline IHD. Neither FVIIIc nor VWF act was significantly related to incident IHD

following adjustment for VWF Ag. We therefore suggest that the associations between these three measurements of the **factor VIII/VWF complex** and incident IHD might have at least three explanations: VWF Ag is a marker of arterial endothelial disturbance; VWF act promotes platelet adhesion/aggregation and hence the platelet component of arterial thrombosis; and FVIIIc promotes fibrin formation and hence the fibrin component of arterial thrombosis.

ACCESSION NUMBER: 1999:358232 SCISEARCH

THE GENUINE ARTICLE: 192CP

TITLE: Factor VIII, von Willebrand factor and the risk of major ischaemic heart disease in the Caerphilly Heart Study

AUTHOR: Rumley A; Lowe G D O (Reprint); Sweetnam P M; Yarnell J W G; Ford R P

CORPORATE SOURCE: UNIV GLASGOW, GLASGOW ROYAL INFIRM, DEPT MED, 10 ALEXANDRA PARADE, GLASGOW G31 2ER, LANARK, SCOTLAND (Reprint); UNIV GLASGOW, GLASGOW ROYAL INFIRM, DEPT MED, GLASGOW G31 2ER, LANARK, SCOTLAND; LLANDOUGH HOSP, MRC, EPIDEMIOLOGICAL UNIT S WALES, PENARTH, S GLAM, WALES; SHIELD DIAGNOSTIC LTD, DUNDEE, SCOTLAND; QUEENS UNIV BELFAST, DIV EPIDEMIOLOGICAL, BELFAST, ANTRIM, NORTH IRELAND

COUNTRY OF AUTHOR: SCOTLAND; WALES; NORTH IRELAND

SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (APR 1999) Vol. 105, No. 1, pp. 110-116.

Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE, OXON, ENGLAND.

ISSN: 0007-1048.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 24

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*